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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,660	12/22/2000	Markus Pompejus	BGI-121CP2	1463

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/746,660	POMPEJUS ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-36 and 48-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-36 and 48-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1-6-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 6-17-04.

Claims 28-36, 48-58 are pending in the instant application.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections/Rejections Necessitated by Amendments

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 48-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the same reasons of record set forth in the Office action mailed 12-17-03.

Applicant's arguments filed 6-17-04 have been fully considered but they are not persuasive. Applicants argue that sufficient written description has been provided for variants (e.g. of 90%) or fragments of SEQ ID NO: 1, whereby their expression in appropriate host cells produces fine chemicals. Applicants assert that the written description requirement has been satisfied for the claimed invention because either a representative number of species of the genera claimed (sequence variants of SEQ ID NO: 1 or fragments of SEQ ID NO: 1, which, when recombinantly expressed, produce fine chemicals in a host cell), or the structural features common to a substantial portion of the genera claimed have been defined in the instant specification, for instance at

pages 32-47 of the instant specification. Contrary to Applicants' assertions, neither adequate definition of a substantial portion of the common structural features of the genera claimed, nor a representative number of species of the genera claimed have been provided in the instant disclosure. The specification teaches SEQ ID NO: 1, encoding SEQ ID NO: 2, its expression in appropriate host cells, and differences obtained in various metabolic pathways or in amino acids produced. The specification also teaches, on pages 32-47 of the instant specification, a general recitation of molecular biology, cloning, subcloning and recombinant expression techniques existing the art, as well as a recitation of percent homologies that may be obtained using further experimentation and using the various sequences disclosed as novel in the instant specification. The specification also contains a recitation of possible fragments that may be obtained and tested for activity upon further experimentation. These prophetic disclosures, however, for future experimentation to obtain putative and previously uncharacterized homologues of SEQ ID NO: 1, or functional fragments thereof, do not provide an adequate number of representatives species for the genera comprising active fragments or homologues of SEQ ID NO: 1, whereby their expression provides for the production of fine chemicals.

Applicants have cited portions of the Revised Interim Written Description Guidelines Training Materials, and argue that adequate representation of species falling within the genus claimed, or adequate definition of the structural features common to a substantial portion of the genus claimed, have been satisfied by the instant disclosure. Applicants argue further that an example of 95% is shown in the

guidelines and should be applicable to the instant application. Contrary to Applicants' assertions, the guidelines provide an example of adequate description of a genus encompassing 95% homology, but in the example provided a specific function is recited in the claims. In the instant application, however, the 95% homology is drawn broadly to a metabolic pathway protein. Metabolic pathway proteins encompass a very broad genus, and no common core structural features (e.g. domain conservation, secondary/higher order structural requirements, motifs) concisely characterize this broad genus. The broad recitation of *encoding a metabolic pathway protein* as functional language does not elucidate what nucleic acid structures encode such and retain 95% homology with SEQ IDN NO: 1 - and further whereby would function in a method for producing any fine chemical. Furthermore, the disclosure of a single sequence (SEQ ID NO: 1) and a generic recitation of how to mutagenize, identify by conventional cloning techniques, and subsequently align sequences obtained using these techniques do not satisfy the written description requirements. The identification of a limited number of species in combination with adequate description of the common features (e.g. minimum domain requirements, mutagenesis data, conserved motifs, required secondary or higher order structures for maintaining enzyme activity) can in some cases satisfy the written description requirements for a genus comprising homologues, but this is not the situation in the instant specification. No evidence has been provided that unambiguously and concisely defines or characterizes the common features comprising homologues of SEQ ID NO: 1 of 90%. The generic molecular biology protocols provided in the instant specification, and in the art, do not provide the

missing details required to adequately define the common features of the genus claimed. Disclosure of a single species does not provide adequate written description for this broader genus. Furthermore, no fragments of SEQ ID NO: 1 have been identified that provide for the production of fine chemicals upon expression in an appropriate host cell. For these reasons, the rejection for lacking adequate written description is maintained.

Claims 28-36, 48-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for altering lysine, homocysteine and methionine metabolism in an isolated host cell (i.e. reduction of lysine, accumulation of homocysteine and methionine) in vitro following transformation of the cell with a nucleic acid comprising SEQ ID NO: 1, encoding SEQ ID NO: 2, does not reasonably provide enablement for a method of producing fine chemicals comprising the transformation of an appropriate host cell with SEQ ID NO: 1 encoding SEQ ID NO: 2, any fragment thereof comprising at least 25 nucleotides or the complement thereof, or any nucleic acid that is 90% homologous to SEQ ID NO: 1 or the complement thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the Office action mailed 12-17-03.

Applicant's arguments filed 6-17-04 have been fully considered but they are not persuasive. Applicants argue that enablement is not precluded by the necessity for

some experimentation, and that any experimentation required to practice the claimed invention constitutes routine and not undue experimentation. Applicants also argue that the instant specification provides the methods for expressing, analyzing and purifying fine chemicals, as well as for generating functional variants and fragments of SEQ ID NO: 1, whereby fine chemicals are produced (i.e. especially on pages 23-39 of the instant specification). Contrary to Applicants' assertions, the ability to generate functional variants or active fragments of the claimed SEQ ID NO: 1, whereby fine chemicals are produced in an appropriate host cell, requires undue experimentation beyond that taught in the instant disclosure. The specification teaches SEQ ID NO: 1, encoding SEQ ID NO: 2, its expression in appropriate host cells, and differences obtained in various metabolic pathways or in amino acids produced. The specification also teaches, on pages 32-47 of the instant specification, a general recitation of molecular biology, cloning, subcloning and recombinant expression techniques existing the art, as well as a recitation of percent homologies that may be obtained using further experimentation and using the various sequences disclosed as novel in the instant specification. The specification also contains a recitation of possible fragments that may be obtained and tested for activity upon further experimentation. These prophetic disclosures, however, for future experimentation to obtain sequence homologues or active subsequences of SEQ ID NO: 1, are not enabling for the ability to practice the invention claimed. The expression of SEQ ID NO: 1, whereby differences obtained in various metabolic pathways or in amino acids produced, is not representative or correlative of the ability to produce fine chemicals comprising the administration of

nucleic acid sequences comprising these proposed homologues or fragments. To determine which homologues or which fragments are functional requires undue experimentation beyond that provided in the instant disclosure, and the recitation of molecular biology techniques well known in the art does not substitute for the undue experimentation required to identify these active fragments or homologues.

The claims are also drawn to the ability to produce fine chemicals comprising the administration of nucleic acids encoding the complement of SEQ ID NO: 1, or fragments thereof. No evidence has been provided in the instant disclosure, however, for the production of any chemicals following the targeting and inhibition of expression of SEQ ID NO: 1. It is unclear how fine chemicals are produced following either overexpression of the claimed nucleic acid, or following its inhibition. No guidance has been provided in the instant disclosure for the generation of fine chemicals upon inhibition of the target SEQ ID NO: 1. The increased expression of SEQ ID NO: 1 in a host cell is not representative or correlative of the inhibition of SEQ ID NO: 1 – It is the opposite. Therefore, the claims are rejected for lacking enablement over the broad scope claimed.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

There is insufficient antecedent basis for "said DNA" in line 1 of claim 54 (inserting –genomic— before "DNA" would be remedial).

In claim 54, lines 1-2, it is unclear what is meant by "said DNA" being "altered by one or more additional metabolic pathway nucleic acid molecules." This phrase can be interpreted in several ways. For instance, it suggests that metabolic pathway nucleic acid molecules perhaps act directly on the DNA and alter it in some way (e.g. degradation, mutation...). It can also be interpreted as meaning that nucleic acid sequences encoding other metabolic pathway proteins are integrated into the genome of the host cell DNA. Appropriate clarification is required.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

JZ
9-12-04